

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Application of: Jerome B. Zeldis                          Confirmation No.: 5112  
Serial No.: 09/734,460                          Art Unit: 1615  
Filed: December 11, 2000                          Examiner: Evans, Charesse L.  
For: Methods and Compositions for                          Attorney Docket No: 9516-018-999  
the Prevention and Treatment of  
Atherosclerosis, Restenosis and  
Related Disorders

**DECLARATION OF DONALD BAIM, M.D. UNDER 37 C.F.R. §1.132**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

I, DONALD BAIM, M.D., do solemnly and sincerely declare and state that:

**I. BACKGROUND**

1. I have never held a position at Celgene. My *curriculum vitae* is attached hereto as Exhibit A.

2. I received an M.D from Yale University School of Medicine in 1975. I received further training in Internal Medicine and Cardiovascular Disease at Stanford University Medical Center through 1981. In 1981, I joined the faculty of Harvard Medical School, where I was appointed as Professor of Medicine in 1994 (a rank which I continue to hold). I established and ran the Interventional Cardiology Program at Beth Israel Hospital from 1981-2000. I am now a senior interventional cardiologist at the Brigham and Women's Hospital, and director of the Center for Integration of Medicine and Innovative Technology (CIMIT) there.

3. I have given over 200 professional presentations, authored or co-authored over 250 publications concerning the treatment of heart disease, atherosclerosis, restenosis, and congestive heart failure. I am editor of the major textbook *Grossman's Cardiac Catheterization, Angiography, and Intervention* (now in its 6<sup>th</sup> edition, 2000)

4. I am skilled in the art of treating heart disease, atherosclerosis, restenosis and congestive heart failure, and am familiar with scientific literature concerning the treatment of the diseases.

5. In sum, I am an expert in the treatment of heart disease, atherosclerosis, restenosis, and congestive heart failure. I have first-hand knowledge of the safety and efficacy of various drugs used to treat these conditions and the problems faced by the pharmaceutical industry in developing new drugs to treat these conditions.

## **II. ATHEROSCLEROSIS, RESTENOSIS AND CONGESTIVE HEART FAILURE ARE DISTINCT DISEASES WHICH OFTEN REQUIRE DIFFERENT TREATMENTS**

6. Atherosclerosis, restenosis and congestive heart failure are *3 different diseases with different etiologies and treatments*. A patient can have any one of these, and not any other (except restenosis which presupposes prior treatment and atherosclerosis). In particular a patient may have congestive heart failure and no atherosclerosis, or atherosclerosis and no congestive heart failure. Treatments like statin drugs effective for reducing atherosclerosis, furthermore, have no effect on restenosis or congestive heart failure, while drugs like angiotensin converting enzyme inhibitors effective for congestive heart failure have no effect on restenosis.

7. Atherosclerosis is a disease of the arteries in which a fatty/wax-like plaque is deposited on the inside of the arterial walls. As the plaque builds up, it causes the arteries to narrow. Over time, this narrowing prevents the blood from flowing properly through the arteries, giving rise to a variety of complications. *Stedman's Medical Dictionary*, 27th Ed., 2000, at page 162. Atherosclerosis is most often treated with the use of lipid-lowering drugs, antiplatelet agents, beta-blockers and blood pressure lowering medications. *Goodman & Gilman's The Pharmacological Basis of Therapeutics*, 9th Ed., 1996.

8. Restenosis is the renarrowing of the arteries as a result of neointimal hyperplasia (scar tissue) that forms to repair damage to the artery caused by previous operations including balloon angioplasty and stent placement. *Stedman's Medical Dictionary*, 27th Ed., 2000, at page 1556. Restenosis is most often treated with repeated angioplasties, coronary artery bypass or insertion of a coronary stent. *Goodman & Gilman's The Pharmacological Basis of Therapeutics*, 9th Ed., 1996. Restenosis after a stent is usually treated by intracoronary brachytherapy (radiation)

9. Congestive heart failure is a condition in which the heart is unable to maintain an adequate circulation of blood in the bodily tissues or to pump out the venous blood returned to it by the veins. Congestive heart failure is treated with diuretics,

angiotensin converting enzyme inhibitors, vasoregulators, beta-blockers and surgery. *Goodman & Gilman's The Pharmacological Basis of Therapeutics*, 9<sup>th</sup> Ed., 1996. There are a number of distinct causes which may lead to congestive heart failure, such as alcohol abuse, drug abuse, hyperthyroidism, viral infection, myocarditis and extreme vitamin deficiency.

### **III. THE '460 APPLICATION**

10. I have read and understand the above-identified U.S. patent application, serial no. 09/734,460 ("the '460 application") and what I understand are its pending claims, which are directed to the use of a certain class of compounds for the treatment and prevention of atherosclerosis and restenosis.

11. I have also read and understand United States Patent No. 5,635,517 to Muller *et al.* ("the '517 patent"), which discloses a class of compounds for the treatment of various diseases related to undesired angiogenesis. One of the diseases listed in the '517 patent is congestive heart failure. The class of compounds disclosed in the '517 patent is much smaller than the class disclosed in the '460 application.

12. I have also read and understand the office actions mailed November 20, 2002 and May 21, 2003, and the Applicant's responses filed February 20, 2003 and July 18, 2003, in connection with the '460 application.

### **IV. THE CLAIMS PENDING IN THE '460 APPLICATION ARE NOT OBVIOUS**

13. In the office actions of November 20, 2002 and May 21, 2003, the Examiner contends that congestive heart failure is so similar to atherosclerosis and/or restenosis as to render the claimed invention obvious. I believe that the Examiner's contention is incorrect.

14. As discussed above, the etiologies of atherosclerosis, restenosis and congestive heart failure are distinct. Moreover, the methods used to treat atherosclerosis, restenosis and congestive heart failure are distinct. Consequently, a treatment that is effective for one disease is not necessarily effective for the treatment of another. In particular, the fact that a compound can be used to treat congestive heart failure does not mean that the compound can be used to treat atherosclerosis or restenosis, or vice versa.

15. Prior to December 11, 2000, which I understand is the filing date of the '460 application, I would not have thought that the compounds disclosed in the '517 patent are necessarily effective for the treatment or prevention of atherosclerosis or restenosis. This is because the '517 patent does not describe the treatment of those diseases, and because I

understood that compounds that can be used to treat or prevent congestive heart failure do not necessarily work for the treatment or prevention of atherosclerosis or restenosis. I believe that others of ordinary skill in the art would have believed the same.

16. In sum, atherosclerosis, restenosis and congestive heart failure are distinct diseases, and the disclosure that a compound can be used to treat congestive heart failure is, in and of itself, not enough for one of ordinary skill in the art to conclude that it can be used to effectively treat atherosclerosis and/or restenosis.

All statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true. All statements made herein are made with the knowledge that willful false statements and the like are punishable by fine or imprisonment, or both, under §1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

IN TESTIMONY WHEREOF, I hereunto set my hand and seal the day and year set opposite my signature.

Dated: November 18, 2003



L.S.  
Donald S. Baim, M.D.

State of Massachusetts

SS.:266-86-2215

County of Middlesex

On Nov 18, 2003, before me, Joanne Buonfiglio Notary Public, personally appeared DONALD BAIM, M.D., personally known to me on the basis of satisfactory evidence to be the person whose name is subscribed to the within instrument and acknowledged to me that, by his signature on the instrument, she executed the instrument.

WITNESS my hand and official seal



My commission expires April 17, 2009.